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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,933	10/04/2005	Amjad Ali	21150P	6475

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EXAMINER
LOEWE, SUN JAE Y

ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
07/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,933	ALI ET AL.	
	Examiner	Art Unit	
	Sun Jae Y. Loewe	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,17 and 21-23* is/are rejected.

7)☒ Claim(s) *9-16 and 18-20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/13/06,10/4/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

1. The information disclosure statement (IDS) submitted on October 4, 2005 and November 13, 2006 were in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. Accordingly, the information disclosure statements were considered. Signed copies of form 1449 are enclosed herewith.

Claim Objections

2. Claims 9-16 and 18-20 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form.

3. Claims 14, 15 and 16-20 objected to because of the following informalities. Pursuant to MPEP 608.01 (m), each claim must end with a period. Claims 14, 15 and 16-20 are missing the period. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-7, 22 and 23 rejected under 35 USC 112 1st paragraph as failing to comply with the written description requirement.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus …") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

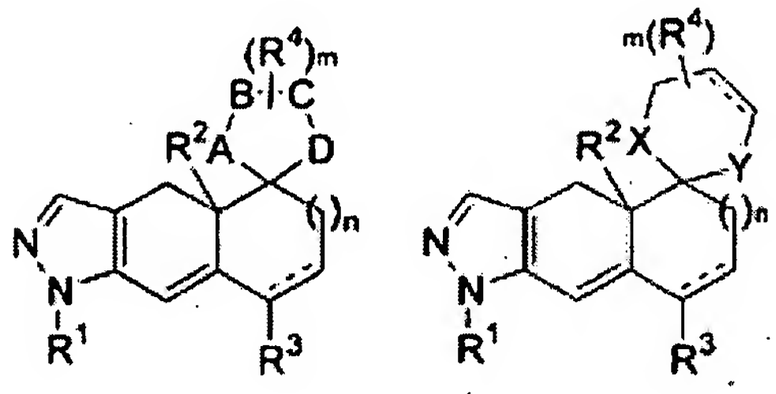
The MPEP states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The Guidelines for Examination of Patent Applications Under 35 USC 112, ¶1, "Written Description" Requirement (Federal Register, Vol. 66, No. 4, pg. 1105, column 3), in accordance with MPEP § 2163, specifically state that for each claim drawn to a genus the written description requirement may be satisfied through sufficient description of a representative number of species by a) actual reduction to practice; b) reduction to drawings or structural chemical formulas; c) disclosure of relevant, identifying characteristics (ie. structure) by functional characteristics coupled with a known or disclosed correlation between function and structure. The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention (Federal Register, Vol. 66, No. 4, p. 1105, 3rd column, 3rd paragraph). Below is such comparison.

It is noted that in the following the comparison is focused on products and not method of use. It is to be understood, however, that a *prima facie* conclusion of lack of written description for product implies the same conclusion for the process of use. In other words, the process of use cannot be practiced in absence of the product.

I. ***Scope of Claims (based on*** elected ***subject matter)***

Compounds of Formula I or II (variables defined in claims 1-7, 22 and 23).



I II

The following variables are claimed *broader* than what is supported by the disclosure (see below section II):

R^1:	for claims 1-5, 22 and 23
R^2 and R^3:	for claims 1-3, 5-7, 22 and 23

II. Scope of Disclosure

Reduction to Practice:

The compounds reduced to practice support the following definitions for R^1-R^3 and n:

R^1:	C_{3-6} cycloalkyl, phenyl, -CH_2-phenyl, pyridyl
R^2:	hydrogen, C_{1-6} alkyl, -CH_2-phenyl, phenyl
R^3:	hydrogen, C_{1-6} alkyl, OR^7

Reduction to Structural or Chemical Formulas:

The only disclosure, in addition to the species reduced to practice, is in form of a *list* of possible substituents for each variable. This type of disclosure is not viewed to be a representation of any of the species it entails. A"laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species. MPEP 2163.I.A. and *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996). Therefore, there is no disclosure of species (eg. by reduction to structural/chemical formulas) in addition to those reduced to practice.

Correlation between Structure and Function:

A structure/activity study (SAR) is disclosed by Smith et al. for a subgenus of the instantly claimed compounds. These studies address the activity of compounds as a function of varying "B-ring size, ketal ring size, and ketal substitution"; however, the substituents corresponding to variables R^1-R^3 were *fixed* in these studies (Smith et al., abstract and Tables 1-3, 5 of pages 2928-2930). Furthermore, the instant specification does not disclose any correlation between function and structure. Thus, it is not understood what *specific structural elements* (pertaining to variables R^1-R^3) are *essential* for the activity of the instantly claimed compounds towards glucocorticoid receptor.

III. Analysis of Fulfillment of Written Description Requirement:

In the absence of a correlation between structure (as it pertains to variables R^1-R^3) and function, it is not possible to predict what modifications will allow for the preservation of the desired activity.

In conclusion: (i) substantial structural variation exists in the genus/subgenus embraced by claims 1-7, 22 and 23; (ii) disclosure of species supporting genus is limited to compounds reduced to practice, which scope is not commensurate with the scope of genus/subgenus claimed; (iii) common structural attributes of the claimed genus/subgenus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art. Thus, the specification fails to provide adequate written description for the genus of compounds claimed and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

(Enablement)

5. Claims 1-7, 22 and 23 rejected under 35 U.S.C. 112, first paragraph.

The specification is *enabling* for the use of the compounds that have adequate written description. The specification is *not enabling* for:

(a) Use of compounds not supported by the disclosure
(b) Method of treating glucocorticoid receptor mediated disease

In conclusion, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to

practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

It is noted that for subsection (b) the arguments are based on the assumption that the compounds are active towards glucocorticoid receptor (ie. compounds that are *supported* by the disclosure). Section (a) is directed only to compounds that are *unsupported* by the disclosure.

The breadth of the claims

(a) The claims are drawn to compounds that are claimed, but not supported by the disclosure.

(b) The claims are drawn to the method of treating glucocorticoid receptor mediated disease/condition using instantly claimed compounds.

The nature of the invention

(a) The genus of compounds are disclosed to show activity towards glucocorticoid receptor.

(b) Claims to the method of use are supported solely by the activity of the compounds towards glucocorticoid receptor.

The state of the prior art/level of ordinary skill/level of predictability

(a) The level of ordinary skill is high, but the level of predictability in the art is low. As discussed in section 4, it is not known what structural limitations are essential to the activity of the compounds towards glucocorticoid receptor. In the absence of further guidance, or structure-activity correlation studies, one of ordinary skill would not expect that the entirety of compounds embraced by the genus would possess the claimed activity. One of ordinary skill would not know which of the compounds not exemplified, if any, would possess the claimed activity.

(b) The state of the art for treatment of glucocorticoid receptor mediated disease by the class of compounds that embraces the instant invention (ie. selective glucocorticoid receptor agonists) is described by Schacke et al. Currently, all compounds that target the instantly claimed process of use are in preclinical studies (Schacke et al., Table 1, page 18 of 20). Thus, there is no art-recognized correlation between glucocorticoid receptor mediation and treatment of any disease.

Furthermore, the level of unpredictability in the art for treating conditions via the etiological pathway of glucocorticoid receptors; ie. interference with pro-inflammatory TNF-α and IL-6 (Schacke et al., p. 10 of 20; Smith et al., p. 2930, 2nd column) is low. See illustrative points below:

- Multiple mediators are involved in inflammatory conditions such as asthma and chronic obstructive pulmonary disease. Due to the redundancy of the mediator effects, it is unlikely that targeting a single mediator will produce a major clinical benefit (Barnes, p. 541, 1st column, 3rd paragraph; McCulloch et al., p. 865, 2nd column, 1st paragraph). For example, in clinical trials targeting the treatment of rheumatoid arthritis using TNF-α inhibition, 30% of individuals failed to respond (McCulloch et al., p. 865, 2nd column, 1st paragraph).

- Although an association between inflammation and cancer has been proposed, the cause and effect remains to be proven (Shacter et al., reviewers comments, p. 25 of 26, 2nd paragraph). Furthermore, multiple etiologies (ie. genetic basis for susceptibility vs. inflammatory basis - Shacter et al., p. 3 of 26) and intertumoral heterogeneities (Zips et al., p.2, 2nd column, 1st paragraph) are suggested in the art for tumor development. Therefore, targeting an inflammatory mediator (eg. indirectly by mediating glucocorticoid receptor) does not necessarily treat a specific type, or more broadly all types, of cancer.

The amount of direction provided by the inventor/existence of working examples

(a)-(b) No direction or working examples

The quantity of experimentation needed to make or use the invention

(a) It is not known which of the unrepresented compounds meet the requirement for activity towards glucocorticoid receptor. It would require undue experimentation for one of ordinary skill to first test which of the compounds possess this activity before being able to practice the invention commensurate in scope with the breadth of the instant claims.

(b) Absent guidance and/or art recognized correlation between activity towards glucocorticoid mediators and treatment of the diseases claimed, particularly in view of the unpredictability in the art, one of ordinary skill is not enabled to practice the claimed invention. The amount of experimentation is deemed to be undue.

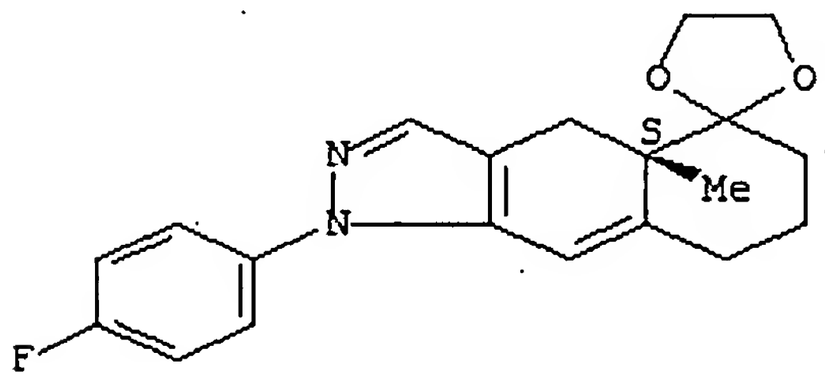
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

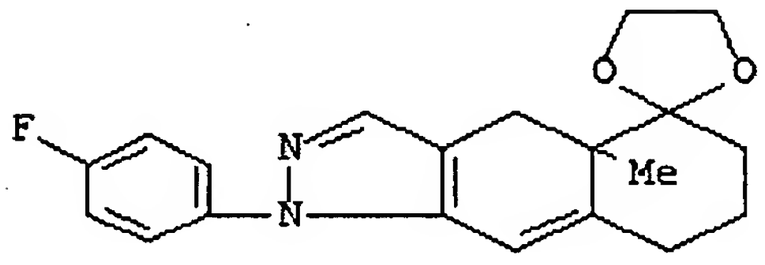
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-4, 6-8, 17, 21 and 22 rejected under 35 U.S.C. 102(e) as being anticipated by Ali et al. US2005/0256315 (page 18).



Formula I: R^1=fluoro substituted phenyl; R^2 = methyl; R^3 = hydrogen; n = 1; -A-B-C-D- = -O-CH_2-CH_2-O.

7. Claims 1-4, 6-8, 17, 21 and 22 rejected under 35 U.S.C. 102(e) as being anticipated by Scanlan et al. US2005/0054799 (Figure 6).



Formula I: R^1=fluoro substituted phenyl; R^2 = methyl; R^3 = hydrogen; n = 1; -A-B-C-D- = -O-CH_2-CH_2-O.

Note: It is commonly known in the art that the synthesis of organic compounds containing a chiral carbon atom yields racemic mixtures, ie. mixtures with equal amounts of the left and right handed enantiomers (http://en.wikipedia.org/wiki/Racemic_mixture). Because the compound taught by Scanlan et al. contains a chiral carbon atom, it occurs as a racemic mixture that necessarily contains the enantiomer of instant claim 17. Thus, the reference anticipates the instant claims.

Conclusions

8. No claims allowed.

9. Any inquiry concerning this communication should be directed to Sun Jae Y. Loewe whose telephone number is 571-272-9074. The examiner can normally be reached on Monday through Friday from 7:30 am to 5:00 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor Joseph McKane can be reached at (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For

more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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